

(c) the fever resembles closely that of other infections; (d) the leukocytosis; (e) the exudate when serous surfaces are involved.

7. The specific organism has not been isolated. A detailed report will appear later to support this.

In concluding, I wish to thank Dr. Warren and Dr. Mann who have made this work possibly by their statistics and coöperation, and Dr. McCreery for his earlier work on the histories.

### THE CITRATE METHOD OF BLOOD TRANSFUSION IN CHILDREN.

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THE citrate method of blood transfusion which I described in January, 1915,<sup>1</sup> has rapidly gained great popularity. Theoretical objections against the mixture of blood with an anticoagulating substance have been overcome by practical experience. This has proved that the citrated blood is clinically as effectual as pure blood. The great simplicity of the method, which makes blood transfusion technically as easy as an ordinary saline infusion, has, of course, widened the applicability of the former, even in smaller communities, and will certainly serve to popularize blood transfusion.

The effectiveness of citrate of soda as an anticoagulant is, of course, nothing new. In fact, we all know that for many years it has been used quite extensively in the laboratories for the purpose of preventing blood from clotting. The dose used for this purpose was 1 per cent.

I have often wondered why so much time has been spent in devising technically most complicated methods (vessel anastomosis, syringes, etc.) instead of applying this well-known drug in human blood transfusion.

The answer is given in the experimental part of my work, which I published in detail a few months ago.<sup>2</sup> These experiments brought to light two important facts:

1. That it is unnecessary to use 1 per cent. sodium citrate to prevent coagulation of the blood, but that 0.2 per cent. suffices.
2. That sodium citrate used at the ratio of 1 per cent. would prove fatal in large transfusions of blood (1000 c.c.).

This last fact answers the question why sodium citrate has not been applied before in human blood transfusion. The fear that this anti-coagulant might prove to be toxic when used in large doses is

<sup>1</sup> Med. Rec., New York, 1915, lxxxvii, 141.

<sup>2</sup> Surg., Gynec. and Obstet., 1915, xxi.

a well-founded one. That sodium citrate may be safely applied for intravenous injection of large quantities of blood, without risk or danger to the patient is based on the fact that my experiments showed that a mixture of 0.2 per cent. citrate of soda is sufficient to prevent coagulation.

These results of my animal experiments were of special importance on account of another publication on this subject which appeared contemporaneously with mine. Weil<sup>3</sup> reported that he had injected up to 350 c.c. of blood mixed with 3.5 grams of sodium citrate. He had used this large dose of citrate because, evidently through some error in his experiments, he had come to the conclusion that 1 per cent. sodium citrate (*i. e.*, the dose used in laboratory work) was necessary to prevent coagulation. There was no warning in his paper against the possible toxicity of sodium citrate at the 1 per cent. ratio. My animal experiments show conclusively that if anybody had applied Weil's dose for a large transfusion on the human being the results would have been fatal. The citrate method, which has proved harmless and efficient, when applied at the 0.2 per cent. ratio, would surely have been abandoned after a few trials if my experiments had not pointed out the toxicity of Weil's dose and thus prevented others from using citrate at the ratio of 1 per cent.

The atoxicity of sodium citrate at the 0.2 per cent. ratio (*i. e.*, 2 grams of sodium citrate to 1000 c.c. of blood) is best proved by the use of this method for transfusion of blood in small children. Blood transfusion in infants has great possibilities. Melena neonatorum, primary and secondary anemias, typhoid hemorrhages, some cases of marasmus, etc., yield remarkably well to blood transfusions and often show most startling results. All the older methods presented the greatest technical difficulties when applied in these little infants, and therefore blood transfusion has not been used sufficiently in small children.

The technic is exactly the same as described for adults.<sup>4</sup> The donor's vein can be punctured proximally or distally, the direction to be chosen according to the individual case, whichever way the blood runs with the greatest facility into the glass receptacle. The blood is mixed in the glass jar with a 2 per cent. sterile solution of sodium citrate at the ratio of 1 to 10 (*i. e.*, 10 parts of solution to 100 c.c. of blood). For the reintroduction of the blood a very fine needle or cannula can be chosen. Thus one can inject the blood even in small children through a superficial arm vein of the finest caliber. This obviates any extensive dissection. By using so fine a needle one assures the slow injection of the blood and prevents the danger of sudden overloading of the circulatory system. The salvarsan flask is attached to a stand and the blood

<sup>3</sup> Jour. Amer. Med. Assn., 1915, lxiv, 425; Clin. Conf., Mt. Sinai Hosp., Jan., 1915.

<sup>4</sup> Loc. cit.

allowed to run into the vein drop by drop (in 1 case the injection of 350 c.c. thus took nearly an hour, and the three-year-old child stood this rather large quantity of blood very well, just on account of the slow injection).

➤ Among the 30 cases of blood-transfusion in which I used the citrate method 7 were children.

The first child in whom the new method was applied was a boy, aged five years, with extensive burns. He received two transfusions of 150 c.c. of blood. His hemoglobin was raised from 42 to 72 per cent. The improvement in the general condition of the child was most remarkable.

The second case was a child, aged three years, with hemorrhages from the intestinal tract. This child received its first transfusion (Lindeman's method) in August, 1914. The hemorrhages then stopped for six months. The patient was readmitted to the hospital in February, 1915, on account of the recurrence of hemorrhages. A second transfusion of 200 c.c. of blood (citrate method) from the father of the child failed to stop the hemorrhages. An exploratory laparotomy was then decided upon, preceded by another transfusion of 450 c.c. of citrated blood. An exploration of the stomach and duodenum was negative. Two weeks later the hemorrhages began again, and since the child was very anemic, another transfusion was advised; this time the Unger method was used. The improvement following this transfusion was only temporary and a fifth transfusion (citrate method) was given in May, 1915. Since then the child has picked up wonderfully. The hemorrhages have stopped entirely. The child appears to be in perfect health; but palpation of the abdomen now reveals an enlarged spleen. This probably explains the hemorrhages from the stomach. This case shows how much can be accomplished by repeated blood transfusions. In regard to the new method it shows that citrated blood is as efficient as unmixed blood. The reason that the clinical result of the last transfusion was so much better than that of the three previous transfusions (two done with the citrate method and one with the Unger method), is probably based on the fact that the blood of the last donor was exceptionally well adapted for this child's blood. We know very little about the relative values of the blood of different donors. But it certainly is advisable, in cases where one transfusion failed to give good results, to try another donor.

The third case was a child, aged six months, suffering from an aplastic anemia. The child received two transfusions, each of 100 c.c. The baby had remarkably improved and showed an excellent color. The child was readmitted two weeks later on account of severe gastro-enteritis, to which it succumbed on August 15, 1915. In little infants a small amount of blood ought to be introduced repeatedly in order to safeguard against sudden overloading of the circulatory system.

The fourth case was a nine-months-old baby; the indication for transfusion was a severe anemia. The child received 100 c.c. of blood and the hemoglobin was raised from 16 to 26 per cent. The child's condition was decidedly improved. This was the only case in this series which had quite a severe reaction (rise of temperature to 102° F. without chill) following the transfusion.

The fifth case seems to me to be the most interesting in this series. A seven-year-old girl had profuse intestinal hemorrhages on the fourteenth day of typhoid fever. The hemorrhages were so profuse that the child was in a dying condition; she was unconscious and the radial pulse was not palpable. An immediate transfusion was done; the blood was taken from the mother; 400 c.c. of blood were transfused. The change in the condition of the child was most remarkable. She reacted while she was receiving the blood and the pulse reappeared. The hemorrhages stopped and no further bleeding occurred during the course of the illness. The disease ran a very severe course, and to combat the marked sepsis a second transfusion was deemed advisable. This was again done by the citrate method, three weeks after the first transfusion. The symptoms of severe typhosepsis were not changed by this transfusion and the child died seven weeks after the onset of her illness. It is interesting to note that this child had a very marked anaphylactic reaction after the first transfusion, though the blood was taken from the mother. No reaction occurred after the second transfusion, for which a professional had been selected and properly tested. This case tends to show that theoretical objections against citrated blood are not based on facts; on the contrary, the citrate transfusion ought to be the method of choice in hemorrhages, because the coagulation time of the recipient's blood is shortened immediately after the introduction of citrated blood.

The sixth case was a three-year-old boy, a hemophiliac, who was very much exsanguinated from a severe hemorrhage (bite on the tongue) which had lasted for twenty-four hours. He received 250 c.c. of citrated blood and the bleeding stopped immediately; his hemoglobin was raised from 19 to 39 per cent.

The last case, the youngest in this series, was a baby, aged twenty days, which had been bleeding since its birth from the umbilicus; 80 c.c. of citrated blood stopped the hemorrhages immediately and permanently; the baby was taken home a few days later.